REMARKS

Claims 1-26 are currently under examination as they read on a method for reducing ocular inflammation comprising administering an agent that neutralizes CXCL 10, wherein the agent reads on an CXCL 10 antibody. The elected species is HSV infection. Claims 27-45 have been withdrawn from further consideration pursuant to 37 C.F.R §1.142(b) as being drawn to a non-elected invention.

Claims 11, 12, 24 and 25 have been amended to replace the term "fragment" with the term "antigen-binding fragment" to more succinctly define the claimed invention. Support for the amendment can be found throughout the specification as filed, for example, at page 20, line 31 to page 21, line 3. Entry of the amendment is respectfully requested.

Regarding 35 U.S.C. § 112, Second Paragraph

Applicants respectfully traverse the rejection of claims 11-12 and 24-25 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Claims 11-12 and 24-25 have been amended herein to clarify that the fragment is an "antigen-binding fragment." In view of the amendment, Applicants respectfully request removal of the rejection of claims 11-12 and 24-25 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.

Regarding 35 U.S.C. § 103

Applicants respectfully traverse the rejection of claims 1-26 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Su et al., *Journal of Virology* 70(2):1277-1281(1996) in view of Liu et al., *Journal of Immunology* 167:4091-4097 (2001).

The Office Action alleges that Su et al. disclose a method to reduce ocular inflammation by reducing chemokine expression associated with HSV infection wherein CXCL-10 (aka. IP-10) is one the chemokines expressed during the infection (see page 1279 , Figure 2 and last paragraph of left column). Office Action, p. 4. The Office Action concedes that Su et al. do not disclose using an agent that specifically neutralizes CXCL- 10 to reduce chemokine expression

for treating ocular inflammation. Office Action, p. 4 The Office Action cites Liu et al. for the proposition that it was well known in the art that an anti-CXCL-10 antibody can neutralize CXCL-10 and reduce inflammation in other viral infected subjects as evidenced by Liu et al. Office Action, p. 4

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the pertinent art. 35 U.S.C. § 103(a) (2000); Graham v. John Deere Co., 383 U.S. 1, 13-14 (1966). The U.S. Court of Appeal for the Federal Circuit recently re-iterated the proper standards for making determinations under § 103. In re Kahn, 441 F.3d 977 (Fed. Cir. 2006). First, the scope and content of the prior art is determined, the differences between the prior art and the claims at issue are ascertained along with the level of ordinary skill in the pertinent art. Against this background, a determination is made whether the subject matter would have been obvious to a person of ordinary skill in the art at the time of the asserted invention. Id. at 985 (citing Dann v. Johnston, 425 U.S. 219, 226 (1976) and Graham v. John Deere Co., 383 U.S. 1, 13-14 (1966)).

> To reject claims in an application under section 103, an examiner must show an unrebutted prima facie case of obviousness . . . . On appeal to the Board, an Appellant can overcome a rejection by showing insufficient evidence of prima facie obviousness or by rebutting the prima facie case with evidence of secondary indicia of nonobviousness.
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> Rouffett, 149 F.3d at 1355.

The Federal Circuit has further noted that "[m]ost inventions arise from a combination of old elements and each element may often be found in the prior art." Kahn at 986.

> However, **mere** identification **in the prior art of each element is insufficient to defeat the patentability of the combined subject matter as a whole**. Rather, a party alleging invalidity due to obviousness must articulate the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious.
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> Id. at 986.

For the reasons set forth below, Appellants respectfully submit that the Examiner has presented insufficient evidence of prima facie obviousness. Furthermore, the Examiner has ignored secondary indicia of nonobviousness that successfully rebut any prima facie obviousness.

"A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994); see KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1739-40 (2007) (explaining that when the prior art teaches away from a combination, that combination is more likely to be nonobvious). The Supreme Court in KSR discussed in some detail United States v. Adams, 383 U.S. 39 (1966), stating in part that in that case, "[t]he Court relied upon the corollary principle that when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." 127 S.Ct. at 1740. Accordingly, if such teachings are present and are significant, there may be no reason to make the asserted combination.

The primary reference, Su et al. discusses that it is known in the art that herpes stromal keratitis, a severe inflammatory response to HSV infection, can be prevented by the timely passive transfer of monoclonal antibody specific for viral glycoprotein D (gD). To study how this antibody treatment prevents excessive corneal inflammation, the authors investigated whether chemokine mRNA expression is inhibited by antibody treatment. To this end, the authors initially detected constitutive mRNA levels for IP-10, KC, MIP-2, MCP-1, MIP-1β, and RANTES in uninfected corneas of BALB/c mice. The authors report that HSV-1 infection resulted in prolonged enhanced chemokine message expression. The authors ultimately analyzed the kinetics of mRNA accumulation for each individual chemokine and concluded:

> Interestingly, anti-gD treatment had **no detectable effect on mRNA expression for IP-10**, KC and RANTES. These results, representative of three independent experiments, indicate that **protective antibody therapy was associated with the downregulation of selected chemokine message** in the HSY-infected corneas.
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> Su et al., p. 1279, left column, second paragraph.

Thus, Su et al. report that the mediation of the HSV associated inflammation by protective antibody therapy did **not** involve IP-10, KC or RANTES. The authors conclude accordingly:

> Protective antibody therapy is associated with reduction in message for MIP-2, MCP-1, MIP-1α andMIP-1β. This result suggests that these four chemokines are the most likely to be involved in the recruitment and activation of leukocytes that subsequently damage the cornea and cause loss of vision.
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> Su et al., p. 1280, right column, final paragraph.

Overall, the Su et al. paper concludes that there is no involvement of IP-10 in the recruitment and activation of leukocytes associated with inflammation caused HSV. The Su et al. reference, far from providing motivation, expressly teaches away from IP-10 as a neutralization target for reducing ocular inflammation in an individual susceptible to ocular inflammation in HSV.

Applicants respectfully request removal of the rejection of claims 1-26 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Su et al., *Journal of Virology* 70(2):1277-1281(1996) in view of Liu et al., *Journal of Immunology* 167:4091-4097 (2001).

CONCLUSION

In light of the Remarks herein, Applicant submits that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP

/Astrid R. Spain/

Astrid R. Spain
Registration No. 47,956

11682 El Camino Real, Suite 400
San Diego, CA 92130
Phone: 858.720.3300 ARS:cjh
Facsimile: 858.720.7800
Date: July 7, 2009

Please recognize our Customer No. 41552 as our correspondence address.